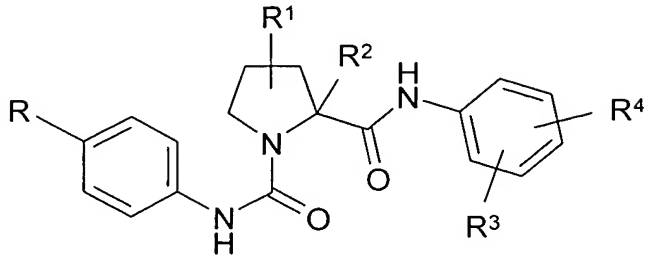
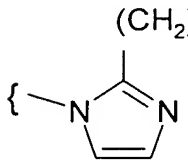
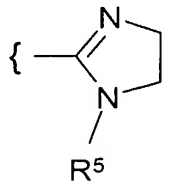
Patent Claims

1. Compounds of the formula I



I

in which

R	denotes Hal, -C≡C-H, -C≡C-A or OA,
R^1	denotes H, =O, Hal, A, OH, OA, A-COO-, Ph-$(CH_2)_n$-COO-, cycloalkyl-$(CH_2)_n$-COO-, A-CONH-, A-CONA-, Ph-CONA-, N_3, NH_2, NO_2, CN, COOH, COOA, $CONH_2$, CONHA, $CON(A)_2$, O-allyl, O-propargyl, O-benzyl, =N-OH, =N-OA or $=CF_2$,
R^2	denotes H or A,
Ph	denotes phenyl which is unsubstituted or mono-, di- or trisubstituted by A, OA, OH or Hal,
R^3	denotes H, Hal or A,
R^4	denotes $-C_6H_4-(CH_2)_n-NR^5R^{5'}$, $-C(=NR^5)NR^5R^{5'}$,  or  ,
R^5, $R^{5'}$	each, independently of one another, denote H or A,
A	denotes unbranched, branched or cyclic alkyl having 1-12 C atoms, in which, in addition, 1-7 H atoms may be replaced by F and/or chlorine,
Hal	denotes F, Cl, Br or I,
n	denotes 0, 1, 2 or 3,

and pharmaceutically usable derivatives, solvates, salts and stereoisomers thereof, including mixtures thereof in all ratios.

2. Compounds according to Claim 1, in which

R denotes Hal or -C≡C-H,

and pharmaceutically usable derivatives, solvates, salts and stereoisomers thereof, including mixtures thereof in all ratios.

3. Compounds according to Claim 1 or 2, in which

R^1 denotes H, =O, Hal, A, OH or OA,

and pharmaceutically usable derivatives, solvates, salts and stereoisomers thereof, including mixtures thereof in all ratios.

4. Compounds according to one or more of Claims 1-3, in which

R^1 denotes OH or OA,

and pharmaceutically usable derivatives, solvates, salts and stereoisomers thereof, including mixtures thereof in all ratios.

5. Compounds according to one or more of Claims 1-4, in which

R^3 denotes H or Hal,

and the pharmaceutically usable derivatives, solvates, salts and stereoisomers thereof, including mixtures thereof in all ratios.

6. Compounds according to one or more of Claims 1-5, in which

R^5, $R^{5'}$ each, independently of one another, denote H or alkyl having 1, 2, 3, 4, 5 or 6 C atoms,

and pharmaceutically usable derivatives, solvates, salts and stereoisomers thereof, including mixtures thereof in all ratios.

7. Compounds according to Claim 1, in which

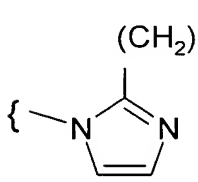
R denotes Hal or -C≡C-H,

R^1 denotes OH or OA

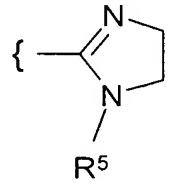
R^2 denotes H or A,

R^3 denotes H or Hal,

R^4 denotes $-C_6H_4-(CH_2)_n-NR^5R^{5'}$, $-C(=NR^5)NR^4R^{5'}$,



or



,

R^5, $R^{5'}$ each, independently of one another, denote H or A,

A denotes unbranched, branched or cyclic alkyl having 1-12 C atoms, in which, in addition, 1-7 H atoms may be replaced by F and/or chlorine,

Hal denotes F, Cl, Br or I,

n denotes 0, 1, 2 or 3,

and pharmaceutically usable derivatives, solvates, salts and stereoisomers thereof, including mixtures thereof in all ratios.

8. Compounds according to Claim 1 selected from the group

N-1-[(4-chlorophenyl)]-N-2-{[4-(2-{dimethylaminomethyl}-phenyl)phenyl]}-(2R,4R)-4-hydroxypyrrolidine-1,2-dicarboxamide,

N-1-[(4-ethynylphenyl)]-N-2-{[4-(2-{dimethylaminomethyl}-phenyl)phenyl]}-(2R,4R)-4-hydroxypyrrolidine-1,2-dicarboxamide,

N-1-[(4-chlorophenyl)]-N-2-{[2-fluoro-4-(2-{dimethylaminomethyl}phenyl)phenyl]}-(2R,4R)-4-hydroxypyrrolidine-1,2-dicarboxamide,

N-1-[(4-ethynylphenyl)]-N-2-{[2-fluoro-4-(2-{dimethylaminomethyl}phenyl)phenyl]}-(2R,4R)-4-hydroxypyrrolidine-1,2-dicarboxamide,

N-1-[(4-chlorophenyl)]-N-2-[(4-(2-dimethylaminomethylimidazol-1-yl)phenyl)]-(2R,4R)-4-hydroxypyrrolidine-1,2-dicarboxamide,

N-1-[(4-ethynylphenyl)]-N-2-[(4-(2-dimethylaminomethyl-imidazol-1-yl)phenyl)]-(2R,4R)-4-hydroxypyrrolidine-1,2-dicarboxamide,

N-1-[(4-chlorophenyl)]-N-2-[(2-fluoro-4-(2-dimethylaminomethyl-imidazol-1-yl)phenyl)]-(2R,4R)-4-hydroxypyrrolidine-1,2-dicarboxamide,

N-1-[(4-ethynylphenyl)]-N-2-[(2-fluoro-4-(2-dimethylamino-methylimidazol-1-yl)phenyl)]-(2R,4R)-4-hydroxypyrrolidine-1,2-dicarboxamide,

N-1-[(4-chlorophenyl)]-N-2-[(4-(*N*,*N*-dimethylamidino)phenyl)]-(2R,4R)-4-hydroxypyrrolidine-1,2-dicarboxamide,

N-1-[(4-ethynylphenyl)]-N-2-[(4-(*N*,*N*-dimethylamidino)phenyl)]-(2R,4R)-4-hydroxypyrrolidine-1,2-dicarboxamide,

N-1-[(4-chlorophenyl)]-N-2-[(2-fluoro-4-(*N*,*N*-dimethylamidino)-phenyl)]-(2R,4R)-4-hydroxypyrrolidine-1,2-dicarboxamide,

N-1-[(4-ethynylphenyl)]-N-2-[(2-fluoro-4-(*N*,*N*-dimethyl-amidino)phenyl)]-(2R,4R)-4-hydroxypyrrolidine-1,2-dicarboxamide,

N-1-[(4-chlorophenyl)]-N-2-[(4-(1-methyl-4,5-dihydro-1*H*-imidazol-2-yl)phenyl)]-(2R,4R)-4-hydroxypyrrolidine-1,2-dicarboxamide,

N-1-[(4-chlorophenyl)]-N-2-[(2-fluoro-4-(1-methyl-4,5-dihydro-1*H*-imidazol-2-yl)phenyl)]-(2R,4R)-4-hydroxypyrrolidine-1,2-dicarboxamide,

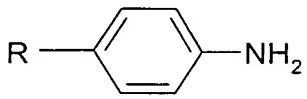
N-1-[(4-ethynylphenyl)]-N-2-[(4-(1-methyl-4,5-dihydro-1*H*-imidazol-2-yl)phenyl)]-(2R,4R)-4-hydroxypyrrolidine-1,2-dicarboxamide,

N-1-[(4-ethynylphenyl)]-N-2-[(2-fluoro-4-(1-methyl-4,5-dihydro-1*H*-imidazol-2-yl)phenyl)]-(2R,4R)-4-hydroxypyrrolidine-1,2-dicarboxamide,

and pharmaceutically usable derivatives, solvates, salts and stereoisomers thereof, including mixtures thereof in all ratios.

9. Process for the preparation of compounds of the formula I according to Claims 1-8 and pharmaceutically usable derivatives, solvates, salts and stereoisomers thereof, characterised in that

a) a compound of the formula II

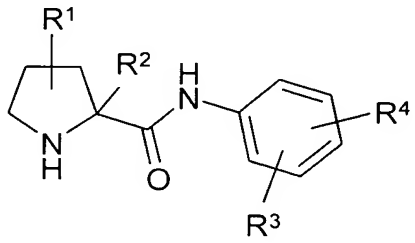


II

in which R has the meaning indicated in Claim 1,

is reacted with a chloroformate derivative to give an intermediate carbamate derivative,

which is subsequently reacted with a compound of the formula III



III

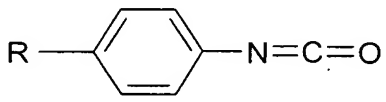
in which

R^1, R^2, R^3 and R^4 have the meaning indicated in Claim 1,

or

b) a compound of the formula III

is reacted with a compound of the formula IV

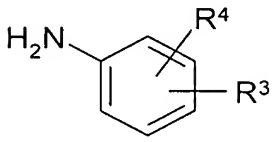


IV

in which
R has the meaning indicated in Claim 1,

or

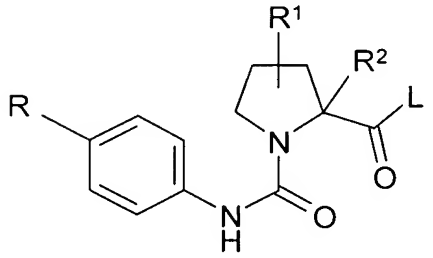
c) a compound of the formula V



V,

in which R^3 and R^4 have the meaning indicated in Claim 1,

is reacted with a compound of the formula VI



VI

in which
L denotes Cl, Br, I or a free or reactively functionally modified OH group and
R, R^1 and R^2 have the meanings indicated in Claim 1,

and/or
a base or acid of the formula I is converted into one of its salts.

10. Compounds of the formula I according to one or more of Claims 1 to 9 as inhibitors of coagulation factor Xa.

11. Compounds of the formula I according to one or more of Claims 1 to 9 as inhibitors of coagulation factor VIIa.

12. Medicaments comprising at least one compound of the formula I according to one or more of Claims 1 to 9 and/or pharmaceutically usable derivatives, solvates, salts and stereoisomers thereof, including mixtures thereof in all ratios, and optionally excipients and/or adjuvants.

13. Medicaments comprising at least one compound of the formula I according to one or more of Claims 1 to 9 and/or pharmaceutically usable derivatives, solvates, salts and stereoisomers thereof, including mixtures thereof in all ratios, and at least one further medicament active ingredient.

14. Use of compounds according to one or more of Claims 1 to 9 and/or physiologically acceptable salts and solvates thereof for the preparation of a medicament for the treatment of thromboses, myocardial infarction, arteriosclerosis, inflammation, apoplexy, angina pectoris, restenosis after angioplasty, claudicatio intermittens, migraine, tinnitus, tumours, tumour diseases and/or tumour metastases.

15. Set (kit) consisting of separate packs of

(a) an effective amount of a compound of the formula I according to one or more of Claims 1 to 9 and/or pharmaceutically usable derivatives, solvates, salts and stereoisomers thereof, including mixtures thereof in all ratios,

and

(b) an effective amount of a further medicament active ingredient.

16. Use of compounds of the formula I according to one or more of Claims 1 to 9 and/or pharmaceutically usable derivatives, solvates, salts and stereoisomers thereof, including mixtures thereof in all ratios,

for the preparation of a medicament for the treatment of thromboses, myocardial infarction, arteriosclerosis, inflammation, apoplexy, angina pectoris, restenosis after angioplasty, claudicatio intermittens, migraine, tinnitus, tumours, tumour diseases and/or tumour metastases,

in combination with at least one further medicament active ingredient.